REMARKS

The Applicants acknowledge the Examiner's comprehensive Office Action, **a Final Rejection**, with appreciation. Claims 12-23 remain pending in the application. The Office acknowledges the priority claims to French Application FR 00.08791 and International Application PCT/FR01/02169 and also acknowledges that certified copies of the foreign priority documents have been received by the Office. The previous rejections under 35 USC § 112, first and second paragraphs, as well as a prior art rejection under 35 USC § 102(b) have been withdrawn in view of the Applicants' Response and Amendment of December 7, 2006. The Office maintains rejections under 35 USC § 102 and 35 USC § 103. The Office also maintains an obviousness-type double patenting rejection.

Claims 20 and 22-23 remain rejected under 35 USC § 102(a) or 102(e) as being anticipated by Guez, et al. It is the position of the Office that Guez, et al. disclose the "same compound" and its pharmaceutical composition comprising a diuretic, such as indapamide, and that, therefore, the disclosed pharmaceutical composition anticipates the instant pharmaceutical composition comprising the instant γ-crystalline form of perindopril t-butylamine salt and a diuretic, including indapamide. The Office goes on to state that a "side-by-side" comparison disclosing distinctness would obviate the rejection.

Absent literal disclosure of the instant crystalline form, the Applicants can only assume that the Office is speculating under some "inherency" theory. The Applicants respectfully submit that MPEP § 2112 states that, in order to rely on a theory of inherency, the Office must provide "a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." MPEP § 2112 also states that "the fact that a certain result or characteristic may occur or be present in the prior art is not enough to establish the inherency of that result or characteristic."

Guez, et al. disclose pharmaceutical compositions comprised of perindopril and indapamide; however, Guez, et al. do not disclose that the perindopril t-butylamine salt used in the disclosed pharmaceutical compositions is in crystalline form, much less the instant γ-crystalline form. Thus, the Office request for a "side by side comparison" is inappropriate. The Office has not even provided adequate disclosure from which to base a side-by-side comparison. Moreover, the Office has not demonstrated that the "allegedly inherent characteristic" necessarily flows from the teaching of the cited reference, and there is no disclosure in the Guez, et al. reference which suggests a pharmaceutical composition comprising the instant γ-crystalline form.

Therefore, the Applicants respectfully submit that the pharmaceutical compositions comprising the instant γ-crystalline form of perindopril t-butylamine salt are not anticipated by the disclosure of the Guez, et al., reference. Reconsideration and withdrawal of the anticipation rejections is respectfully requested.

Claims 12-18 and 20-23 remain rejected for obviousness under 35 USC § 103(a) based on Vincent, et al. in view of Guez, et al. or Brittain. It is the position of the Office that Guez, et al. disclose the "same compound" and its pharmaceutical composition comprising a diuretic, such as indapamide, and that Vincent, et al. disclose "the same crystalline compound with an unstable status compared with the instant gamma form of the same compound."

The Office goes on to state that "[i]t is well recognized in the art that process of preparing a pharmaceutical composition will produce the most thermodynamically stable form of crystals" and that, therefore, the unstable crystalline form of Vincent, et al. and the instant γ-crystalline form would be converted into the same thermodynamically stable form. The Office maintains that absent a showing of superior properties, the instant γ-crystalline form and its pharmaceutical compositions are obvious based on the disclosure of the cited references.

The Office cites the Brittain reference (pages 348-361) to support its allegation that the instant γ-crystalline form and the crystalline form of Vincent, et al. would convert

to a different, more thermodynamicallly stable form during the process of forming a pharmaceutical compostion.

With the instant Amendment, Claim 20 has been amended to recite a solid pharmaceutical composition. The Applicants respectfully submit that the Office has not demonstrated that the instant γ-crystalline form is tranformed to a different crystalline form in a solid pharmaceutical composition.

Moreover, the Brittain reference states (at page 348) that "[a]s tableting speeds increase towards commercial production, exposure times to stress decrease and one would anticipate even less chance for crystalline conversion. For the production of many substances, this situation is certainly true." The reference goes on to describe a study involving thirty-two (32) drugs known to exist in different polymorphic states. Of these thirty-two (32) drugs, eleven (11) appear to have been designated "transforming substances," and of these eleven (11) substances, detailed studies of tableting were conducted on only three (3) substances. The reference also discloses additional studies done on crystalline forms of other drugs as well as studies done on drugs containing amorphous material. Therefore, the Applicants respectfully reiterate that the Office selective quotation of this comprehensive review of polymorphism is inappropriate and prejudicial to the applicant.

The Applicants respectfully submit that the data for specific compounds (which are structurally unrelated to the instantly claimed γ-crystalline form of perindopril t-butylamine salt) disclosed in the cited reference may not be extrapolated to the instant γ-crystalline form of perindopril t-butylamine salt, and that such data does not support the generalized speculation of the Office with respect to polymorphs. The Applicants further submit that the Office argumentation directed to metastable conversion in formulating a pharmaceutical composition based on the Brittain reference is certainly not relevant to substance/compound and process Claims 12-18.

Moreover, in the preface, Brittain states that "[s]ince the middle of last century it has been noted that organic molecules can be obtained in more than one distinct crystal form..." and that "this book represents an attempt to summarize the major issues pertaining to the pharmaceutical aspects of polymorphism..." Thus, the Applicants respectfully submit that the Brittain reference, when taken as a whole, demonstrates that one skilled in the art would recognize that polymorphs are distinct substances which possess distinct physical and structural properties. The very existence of the Brittain reference demonstrates that polymorphs are characterized as different substances.

As noted above with respect to the anticipation rejection, the Applicants respectfully submit that MPEP § 2112 states that "the fact that a certain result or characteristic may occur or be present in the prior art is not enough to establish the inherency of that result or characteristic" and that the Office must provide "a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." The Office has already acknowledged that Vincent, et al. do not disclose the instant γ-crystalline form of perindopril t-butylamine salt, and the Office has provided no demonstration that Guez, et al. disclose ***any*** crystalline form of perindopril t-butylamine salt. Thus, the Office clearly has not demonstrated that the "allegedly inherent characteristic" necessarily flows from the teaching of the cited reference.

Finally, the Applicants respectfully submit that in a USPTO presentation (available at http://www.cabic.com/bcp/061306/CLow_PPP.ppt and also enclosed with this Response) given on June 13, 2006, Examiner Christopher LOW presented the current USPTO view on polymorphs. This presentation suggests that the current Office position is that a particular polymorph is unobvious based on the unpredictability of its existence and identification.

Thus, the Applicants respectfully submit that the instant γ-crystalline form, the process for making instant γ-crystalline form, as well as the instant pharmaceutical compositions comprising the γ-crystalline form are not rendered obvious by the disclosure of the Vincent, et al., Guez, et al., and Brittain references.

Reconsideration and withdrawal of the obviousness rejection is respectfully requested.

Claims 20-23 are also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1,8-9, and 11-12 of co-pending application US Serial No. 11/052,489 or over Claims 22-23 and 25-26 of co-pending application US Serial No. 10/792,355 in view of Brittain. It is the position of the Office that, although the conflicting claims are not identical, they are not patentably distinct since the instant claims as well as the claims in the co-pending applications are directed to pharmaceutical compositions comprising crystalline forms of perindopril t-butylamine salt.

The Office goes on to state that "[i]t is well recognized in the art that process of preparing a pharmaceutical composition will produce the most thermodynamically stable form of crystals" and that, therefore, the crystalline forms claimed in the co-pending applications and the instant γ-crystalline form would be transformed into the same thermodynamically stable form during the process of preparing a pharmaceutical compostion. The Office again cites the Brittain reference to support this allegation.

As discussed above, the Applicants respectfully submit that the data for specific compounds (which are structurally unrelated to the instantly claimed γ-crystalline form of perindopril t-butylamine salt) disclosed in the cited reference may not be extrapolated to the instant γ-crystalline form of perindopril t-butylamine salt, and that such data does not support the generalized conclusions of the Office with respect to polymorphs. The Brittain reference demonstrates that one skilled in the art would also recognize that different, crystalline forms of the compound would possess distinct physical properties, and it has also been established by the discussion above that the Office recognizes that distinct crystalline forms may represent patentably distinct subject matter.

There is nothing in co-pending application US Serial No. 11/052,489 or in co-pending application US Serial No. 10/792,355 to suggest the particular γ-crystalline

form nor a suitable method for obtaining the instant γ-crystalline form. Moreover, it is established Office policy that polymorphs are distinct inventions. Consequently, the Office rejection contradicts accepted Office policy. Thus, the instant γ-crystalline form of perindopril t-butylamine salt is patentably distinct from the limited disclosures of the α-crystalline and β-crystalline forms of perindopril t-butylamine salt. Reconsideration and withdrawal of the obviousness-type double-patenting rejection is respectfully requested.

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Accordingly, entry the present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,

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THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.